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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/035,301

10/25/2001

Dennis France

4-30944A

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01/05/2010

NOVARTIS INSTITUTES FOR BIOMEDICAL RESEARCH, INC.
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CAMBRIDGE, MA 02139

EXAMINER

KOSAR, ANDREW D

ART UNIT

PAPER NUMBER

1654

MAIL DATE

DELIVERY MODE

01/05/2010

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/035,301	Applicant(s) FRANCE ET AL.	
	Examiner ANDREW D. KOSAR	Art Unit 1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 October 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13 and 15 is/are pending in the application.
- 4a) Of the above claim(s) 1-7, 11 and 12 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 8-10, 13 and 15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 29, 2009 has been entered.

Response to Amendments/Arguments

Claims 1-13 and 15 are pending. Claims 1-7, 11 and 12 remain withdrawn from consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention/species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on April 1, 2008.

Applicant's amendments and arguments filed October 29, 2009 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed below in original or modified form is herein withdrawn.

As previously, Applicant argues that the compounds of Billich, Häbich and Scholz are not for proliferative disorders. In response to applicant's argument that the compounds of the prior art are not taught/suggested to be antiproliferatives, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). Here, a *prima facie* case of obviousness has been set forth where the combination to form new antiviral compounds flows

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logically from the combination of the references. Furthermore, it should be noted that the claims are to compounds/compositions, and not to methods of use.

Further, Applicant argues that the combined teachings of Scholz and Billich teach away from the benzyl derivatives claimed. Applicant asserts the "surprising discovery" is that the 2-hydroxy-4-methoxybenzyl at R4 are "favorable for the treatment of proliferative diseases". Respectfully, again, the claims are drawn to products, and while the use may be unobvious (the method claims are currently withdrawn and have not been considered on the merits), the claims are drawn to compounds and the compounds R4 group is taught by Billich in several compounds, as acknowledged by Applicant in the instant specification. The difference determined and discussed in the obviousness rejection is at the N-terminus of the peptide, not the C-terminus. Modification of the N-terminus of the compound of Billich is obvious in light of the teachings in the art, as previously discussed.

Further, in response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

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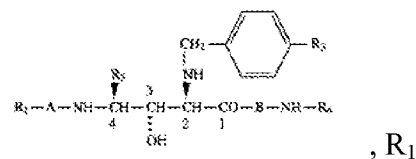
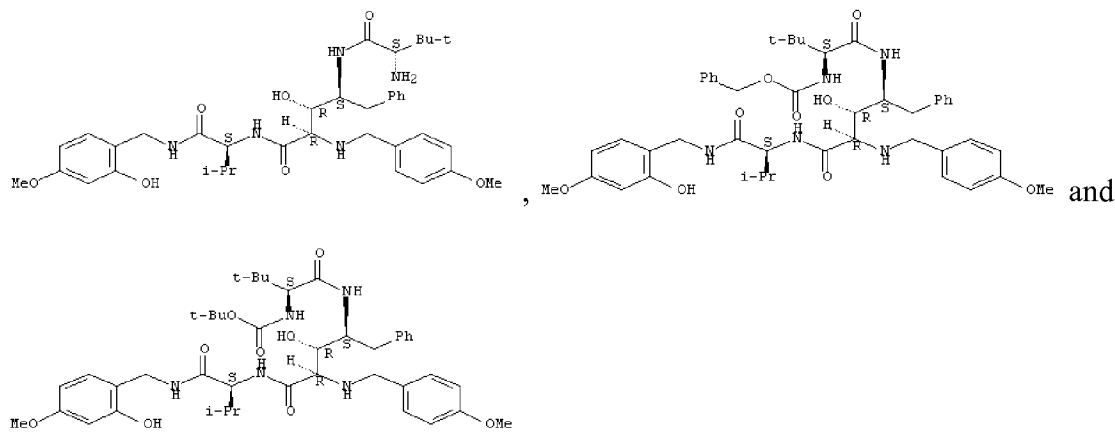
Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 8-10, 13 and 15 remain rejected under 35 U.S.C. 103(a) as being unpatentable over BILLICH (US Patent 5,538,997; IDS 2/26/02) in view of HÄBICH (US Patent 5,633,231) and SCHOLZ (D. Scholz et al. J. Med. Chem. (1994) 37, pages 3079-3089).

As stated in the instant specification, Billich teaches the instantly claimed compound where the only difference is the N-protecting group, e.g. compounds such as:



Billich teaches that in the compounds of the structure:

is an amino protecting group or is of the group R₅Y, where R₅ may be, amongst other options, substituted arylalkyl (column 1, lines 17-25). The compounds of Billich are contemplated as antivirals for HIV (e.g. column 1, lines 36-40).

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Häbich teaches a variety of benzyl esters attached to peptides, including 3-methylbenzylester (e.g. column 53, line 73) attached to the N-terminus of a peptide/peptide like compound. The compounds of Häbich are contemplated as antivirals for HIV (e.g. column 1, lines 8-14).

Scholz teaches HIV antivirals, sharing the core structure of the instant compounds, providing structural analysis of the various positions and their effect on activity (throughout). Scholz determined that the N-terminal protecting group adversely affected the activity when changed from the aryl to alkyl groups, e.g. benzyl to t-butyl (e.g. page 3083, table 4 and discussion). Substitution with 2-pyridine produced a slightly better inhibitor. Scholz states that the R₁ group findings are consistent with the knowledge in the art the HIV P3 site has preference for aromatic residues.

Thus, it would have been obvious to have used any aromatic benzylester, including the 3-methylbenzylester of Häbich on the compounds of Billich, with the expectation that the aromatic compound would function similarly to the benzylester, particularly since Billich teaches that R₁ can be any optionally substituted arylalkyl and teaches the compound with the only difference being the benzylester vs. 3-methylbenzylester.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the foregoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable

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expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANDREW D. KOSAR whose telephone number is (571)272-0913. The examiner can normally be reached on Monday - Friday 08:00 - 16:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Andrew D Kosar/
Primary Examiner, Art Unit 1654